TRANSLATION

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
C1-A0326P		
International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/JP2005/006298	31.03.2005	31.03.2004

International Patent Classification (IPC) or national classification and IPC

A01K67/027, C07K16/18, C12N15/09

Applicant

CHUGAI SEIYAKU KABUSHIKI KAISHA

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ (*sent to the applicant and to the International Bureau*) a total of _____ sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ (*sent to the International Bureau only*) a total of (indicate type and number of electronic carrier(s))
      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☐ Box No. II Priority
   - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☒ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2005/006298

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (Rule 12.3 and 23.1(b))

☐ publication of the international application (Rule 12.4)

☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

☒ the international application as originally filed/furnished

☐ the description:

pages _____ as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

nos. _____ as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* _____ received by this Authority on _____

nos.* _____ received by this Authority on _____

☐ the drawings:

sheets _____ as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing (*specify*): _____

☐ any table(s) related to sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing (*specify*): _____

☐ any table(s) related to sequence listing (*specify*): _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2005/006298

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation to restrict or pay additional fees the applicant has:
   - ☐ restricted the claims.
   - ☐ paid additional fees.
   - ☐ paid additional fees under protest.
   - ☐ neither restricted the claims nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:
   - ☐ complied with.
   - ☒ not complied with for the following reasons:

The feature that is common to claims 1 to 15 is the non-human animal carrying a gene that encodes a soluble form of a membrane protein.

However, transgenic mice carrying a gene that encodes a soluble form of a membrane protein were well known on the priority date of the present application (for example, refer to Int. Immunol., (1999), Vol. 11, No. 3, pages 333 to 339 and J. Immunol., (2001), Vol. 167, No. 8, pages 4321 to 4328, etc.), and thus said technical feature does not define a contribution over prior art in the light of the disclosures in the abovementioned documents. Such being the case, the feature in question cannot be said to be a special technical feature. Furthermore, there is no other relationship involving one or more of the same or corresponding special technical features among the inventions in question.

4. Consequently, this report has been established in respect of the following parts of the international application:
   - ☒ all parts.
   - ☐ the parts relating to claims Nos. _____

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	4-8, 11-15	YES
	Claims	1-3, 9-10	NO
Inventive step (IS)	Claims		YES
	Claims	1-15	NO
Industrial applicability (IA)	Claims	1-15	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Document 1: Y. TAMURA et al., "CD14 transgenic mice expressing membrane and soluble forms: comparisons of levels of cytokines and lethalities in response to lipopolysaccharide between transgenic and non-transgenic mice," Int. Immunol., (1999), Vol. 11, No. 3, pages 333 to 339

Document 2: C. WATANABE et al., "Enhanced immune responses in transgenic mice expressing a truncated form of the lymphocyte semaphorin CD100," J. Immunol., (2001), Vol. 167, No. 8, pages 4321 to 4328

Document 3: W. LU et al., "Characterization of a truncated soluble form of the baculovirus (AcMNPV) major envelope protein Gp64," Protein Expr. Purif., (2002), Vol. 24, No. 2, pages 196 to 201

Document 4: K. L. HEFFERON et al., "Host cell receptor binding by baculovirus GP64 and kinetics of virion entry," Virology (1999), Vol. 258, No. 2, pages 455 to 468

Document 5: Toshihiko OTOMO et al., "Gp64 Hatsugen / CCR2 Knockout Mouse Narabi ni COR2 Hatsugen

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Baculovirus wo Mochiita Kinoteki Kotai no Sakusei," Nihon Bunshi Seibutsu Gakkai Nenkai Program Koen Yoshishu, (2003), Vol. 26, page 660

Document 6: Norio KAMATA et al., "Gp64 Hatsugen Mouse no Sakushutsu Narabi ni Hatsugagata Baculovirus ni Taisuru Tolerance Yudo," Nihon Bunshi Seibutsu Gakkai Nenkai Program Koen Yoshishu (2003), Vol. 26, page 659

Document 7: WO 2003/104453 A1 (Chugai Pharmaceutical Co., Ltd.), 18 December 2003, entire text & AU 2003242024 A1 & EP 1514928 A1

The inventions set forth in claims 1 to 3 and 9 to 10 lack novelty and do not involve an inventive step in the light of document 1 cited in the international search report.

Document 1 presents transgenic mice which express a gene that encodes a soluble form of CD14. Therein, document 1 also indicates that the transgenic mice in question transmitted this CD14 gene to subsequent generations.

The inventions set forth in claims 1 to 2 and 9 lack novelty and do not involve an inventive step in the light of document 2 cited in the international search report.

Document 2 presents transgenic mice which express a gene that encodes a soluble form of CD100.

The inventions set forth in claims 1 to 15 do not involve an inventive step in the light of documents 3 to

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

6 cited in the international search report.

Documents 3 to 4 present the amino acid sequence of soluble gp64 and the base sequence of the gene that encodes the soluble moiety of gp64.

Meanwhile documents 5 to 7 present transgenic mice transfected with the gene that encodes the entire length of gp64, which is a baculovirus membrane protein. Therein, documents 5 to 7 indicate that because such transgenic mice have an immunological tolerance to baculoviruses, it is possible to use said transgenic mice to produce antibodies; furthermore, said documents also indicate that it is possible to produce antibodies that target the membrane protein as a target antigen by using a baculovirus as an immunogen.

Prior to the priority date of the present application, it was common practice to create transgenic mice by transfecting mice with a known gene which encodes a protein that exhibits a given function. Meanwhile, documents 5 to 7 present methods for creating transgenic mice transfected with a gene that encodes a gp64 membrane protein. Such being the case, it would have been easy for a person skilled in the art to conceive of creating transgenic mice which have been transfected with the gene that encodes the soluble gp64 from the inventions presented in documents 3 to 4, and then producing antibodies by means of the transgenic mice obtained in this manner in the light of the disclosures in documents 5 to 7 and the abovementioned well-known techniques.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, Item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☐ in written format

   ☒ in computer readable form

   c. time of filing/furnishing

   ☒ contained in the international application as filed

   ☐ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment* on _____

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

* *If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2005/006298

A. CLASSIFICATION OF SUBJECT MATTER
Int.Cl[7] A01K67/027, C07K16/18, C12N15/09

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
Int.Cl[7] A01K67/027, C07K16/18, C12N15/09

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
BIOTECHNOLOGY ABSTRACT(DIALOG), BIOSIS(DIALOG), MEDLINE(STN), WPI(DIALOG), JSTPlus(JOIS), SwissProt/PIR/GeneSeq, GenBank/EMBL/DDBJ/GeneSeq

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X/A	TAMURA Y., et al., CD14 transgenic mice expressing membrane and soluble forms: comparisons of levels of cytokines and lethalities in response to lipopolysaccharide between transgenic and non-transgenic mice., Int.Immunol., (1999), Vol.11, No.3, p.333-9.	1-3,9-10/ 4-8,11-15
X/A	WATANABE, C. et al., Enhanced immune responses in transgenic mice expressing a truncated form of the lymphocyte semaphoring CD100, J.Immunol., (2001), Vol.167, No.8, p.4321-8.	1-2,9/ 3-8,10-15
Y	LU, W., et al., Characterization of a truncated soluble form of the abculovirus (AcMNPV) major envelope protein Gp64, Protein Expr.Purif., (2002), Vol.24, No.2, pages 196 to 201	1-15

[X] Further documents are listed in the continuation of Box C.

[ ] See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
23 June, 2005 (23.06.05)	12 July, 2005 (12.07.05)
Name and mailing address of the ISA/ Japanese Patent Office	Authorized officer
Facsimile No.	Telephone No.

Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International application No.
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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	HEFFERON, K.L., et al., Host cell receptor binding by baculovirus GP64 and kinetics of virion entry, Virology (1999), Vol.258, No.2, p.455-68	1-15
Y	Toshihiko OTOMO et al., "Gp64 Hatsugen/CCR2 Knockout Mouse Narabini COR2 Hatsugen Baculovirus o Mochiita Kinoteki Kotai no Sakusei", Nihon Bunshi Seibutsu Gakkai Nenkai Program Koen Yoshishu, (2003), Vol.26, page 660	1-15
Y	Norio KAMATA et al., "gp64 Hatsugen Mouse no Sakushutsu Narabini Hatsugagata Baculovirus ni Taisuru Tolerance Yudo", Nihon Bunshi Seibutsu Gakkai Nenkai Program Koen Yoshishu (2003), Vol.26, page659	1-15
Y	WO 2003/104453 A1 (Chugai Pharmaceutical Co., Ltd.), 18 December, 2003 (18.12.03), Full text & AU 2003242024 A1 & EP 1514928 A1	1-15

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2005/006298

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

The matter common to claims 1 to 15 resides in a nonhuman animal carrying a gene encoding a soluble protein of a membrane protein. However, a transgenic mouse carrying a gene encoding a soluble protein of a membrane protein was known in public on the priority date of the present case (see, Int.Immunol (1999), Vol.11, No.3, p.333-9, J.Immunol (2001), Vol.167, No.8, p.4321-8, etc.). Thus, this technical feature does not make a contribution over prior art, considering the disclosures in the above documents, and, therefore cannot be considered as a special technical feature. Furthermore, there is no the same or corresponding special technical feature.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.